

CLAIMS

I claim:

1. A method for screening for a bioactive agent capable of binding to a Toso protein encoded by a recombinant nucleic acid that will hybridize under high stringency conditions to the nucleic acid sequence depicted in Figure 1 (SEQ ID NO:1) or its complement., said method comprising combining a Toso protein and a candidate bioactive agent, and determining the binding of said candidate agent to said Toso protein.
2. A method according to claim 1, wherein said Toso protein is on the surface of a cell.
3. A method according to claim 1, wherein the candidate bioactive agent is labelled.
4. A method according to claim 1, wherein said Toso protein comprises the full length cell surface receptor.
5. A method according to claim 1, wherein said Toso protein comprises the extracellular domain of Toso.
6. A method according to claim 5 wherein said Toso protein further comprises the transmembrane domain.
7. A method according to claim 1, wherein said Toso protein comprises the cytoplasmic domain.
8. A method according to claim 1 further comprising adding a competitor known to bind to said Toso receptor.
9. A method for screening for a bioactive agent capable of modulating the activity of a Toso cell-surface receptor, said method comprising the steps of:
 - a) adding a candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding a Toso receptor;

CA/ 651, 150

Fayan

can re

5/30/98

- Sub
D1
(cont.)
5
- b) exposing said cells to an apoptotic agent that will induce apoptosis; and
 - c) determining the effect of the candidate bioactive agent on apoptosis.

10. A method according to claim 9 wherein a library of candidate bioactive agents are added to a plurality of cells comprising a recombinant nucleic acid encoding a Toso receptor.

11. A method according to claim 9 further comprising adding a labeling agent that will label apoptotic cells.

12. A method according to claim 9 further comprising separating the apoptotic cells from the non-apoptotic cells.

10 13. A method according to claim 9 wherein said labeling agent is annexin.

14. A method according to claim 12 wherein said separation is done by FACS.

15. A method according to claim 9 wherein said apoptotic agent is selected from the group consisting of an anti-Fas antibody, TNF- α , FADD, cycloheximide, PMA, ionomycin and chemotherapeutic agents.

15 16. A method of modulating apoptosis in a cell comprising administering to said cell an exogenous compound that binds to a Toso protein wherein said binding modulates the biological activity of said Toso protein.

Sub
D1
20 17. A method of according to claim 16 wherein the binding of said exogenous compound to said Toso protein reduces or eliminates the biological activity of said Toso protein.

18. A method of according to claim 16 wherein the binding of said exogenous compound to said Toso protein increases the biological activity of said Toso protein.

19. A method for identifying a cell containing a mutant Toso gene comprising determining the sequence of all or part of at least one of the endogenous Toso genes.

20. A method of identifying the Toso genotype of an individual comprising determining all or part of the sequence of at least one Toso gene of said individual.

5 21. A method according to claim 19 or 20 further comprising comparing the sequence of said Toso gene to a known Toso gene.

22. A method according to claim 21 wherein a difference in the sequence between the Toso gene of said individual and said known Toso gene is indicative of a disease state or a propensity for a disease state.

10 23. A method for diagnosing an apoptosis related condition in an individual comprising:
a) measuring the activity of Toso in a tissue from a first individual; and
b) comparing said activity to an activity of Toso in a tissue from a second,
unaffected individual or from a second tissue in said first individual;
wherein when the activity of Toso from said first individual is less than the activity of
15 Toso in said second individual, the first individual is at risk for an apoptosis related condition.

24. The method according to Claim 23 wherein said apoptosis related condition is mediated by Fas.

20 25. The method according to Claim 23 wherein said apoptosis related condition is mediated by TNF.

1100
D3